

REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office action dated August 27, 2002 are respectfully requested. Applicants petition the Commissioner for a 2-month extension of time. A separate petition accompanies this amendment.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page(s) is/are captioned "Version With Markings to Show Changes Made."

I. AmendmentsA. In the Specification:

The specification has been amended for clarity and to correct obvious typographical errors.

B. In the Claims:

Claim 1 is amended to recite that the cells are contacted with a compound of interest and a labeled ligand and that the determining is by measuring the amount of labeled ligand bound to the cell. The claim was further amended for clarity and grammar. Support for this amendment can be found in original claim 2.

Claims 2 and 3 stand cancelled.

Claim 7 is amended to clarify that during the adding step, the compound of interest contact the cells in the first channel. Support for this amendment can be found at least on page 17, lines 13-15.

Claims 13 and 16-17 are amended to provide proper antecedent basis.

No new subject matter has been added by way of these amendments.

II. Rejection under 35 U.S.C. §112, second paragraph

Claims 13, and 16-17 were rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject

matter which the applicant regards as the invention. The Examiner had two specific rejections which are set forth and addressed below.

A. Rejection of claim 13

The Examiner objected to the language "agent" allegedly for not providing proper antecedent basis.

Applicants have amended claim 13 to recite a "compound of interest", which finds proper antecedent basis in claim 7.

B. Rejection of claims 16 and 17

The Examiner objected to the language "said compound of interest" allegedly for not providing proper antecedent basis.

Applicants have amended claims 16 and 17 to recite an "agent", which finds proper antecedent basis in claim 14.

In light of the foregoing, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §112, second paragraph.

III. Information Disclosure Statement

The Examiner noted that the listing of references in the specification is not a proper information disclosure statement. Applicants note that all references cited in the specification were submitted for consideration in an Information Disclosure Statement in accord with 37 C.F.R. § 1.97 and § 1.98 on January 12, 2001.

Applicants request the Examiner initial the citations on the Form 1449 if the citations were considered, whether or not the citation conforms with 37 C.F.R. § 1.98, and draw a line through the citation if it is not considered. Applicants further request the Examiner include a copy of the marked Form 1449 with the next communication.

IV. Rejection under 35 U.S.C. § 102

Claims 1-14 and 16-18 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Wu *et al.* (U.S. Patent No. 6,297,061). This rejection is respectfully traversed.

A. The Present Invention

The present invention provides methods for performing cell-based operations capable of identifying single cell status. The method, according to claims 1 and 7, employs a device having a reservoir containing the cells for the cell-based operations, where the reservoir contains an appropriate viable cell supporting medium, a first capillary channel in fluid transfer relationship with said reservoir, an electroosmotic pump comprising a second capillary channel in fluid receiving relationship with the first channel, an electrokinetic medium in the second capillary channel and a pair of electrodes for creating an electrical field in the electrokinetic medium for moving electrokinetic medium in the second channel, and a detector.

The method, according to claim 14, employs fixed cells and a device having a reservoir containing the fixed cells, a capillary channel in fluid transfer relationship with the reservoir, a pair of electrodes for creating an electrical field in a conductive medium, and a detector.

The method, according to claims 1 and 14, comprises (i) at least prior to adding said cells to the reservoir, contacting the cells with an agent that affects the status of the cells; (ii) applying an electrical field to a conductive or electrokinetic medium in the capillary channel (the second capillary channel in claim 1), whereby cells move from the reservoir to the channel (the first channel in claim 1); (iii) moving the cells to the site of the detector; and (iv) determining the effect of the agent on the status of the cells. The method according to claim 1, further includes contacting said cells with a labeled ligand which competes with the compound of interest for binding to a cell receptor and determining the effect of the agent by measuring the amount of labeled ligand bound to the cell.

The method, according to claim 7, comprises (a) applying an electrical field to the electrokinetic medium in the second capillary channel in a direction to remove liquid from the first channel, whereby cells move individually from the reservoir into the first channel;

(b) adding by electrokinetic means into the first channel a compound of interest for contact in the first channel with the cells; (c) moving the cells to the site of the detector; and (d) determining the effect of the compound on the status of the cells.

B. The Prior Art

WU ET AL. describe a method and apparatus for detecting the presence of small particles in a fluid that also comprises larger particles. Wu *et al.* provide for simultaneous filtering of the larger particles and reaction of the small particles. The device of Wu *et al.* uses an "H" shaped reactor. The reactor uses diffusion to separate the small particles from the larger particles. The crossbar of the H is a laminar flow reaction channel. A sample stream and a reagent stream enter through different arms of the H on the upstream end of the crossbar. The analyte particles diffuse from the sample stream into the reagent stream, leaving behind the larger particles in the residual sample stream. The product particles can then be detected in the product stream. The apparatus may further use a second reagent stream that joins the product stream in a "T" configuration. Means for applying pressure to the flow through the device are vacuum exerted by chemical or mechanical means, a column of water or other means of applying water pressure, electroendoosmotic forces, optical forces, gravitational forces, and surface tension forces.

C. Analysis

According to the M.P.E.P. § 2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference".

Wu *et al.* fail to teach element (i) of claims 1 and 14 and element (b) of claim 7.

With regard to element (i), Wu *et al.* teaches that a sample stream and a reagent stream enter through different arms of the H on the upstream end of the crossbar, not prior to adding the sample to the reservoir.

With regard to element (b), as noted above, Wu *et al.* teaches a sample stream and a reagent stream enter through different arms of the H on the upstream end of the

crossbar. Contact of the sample stream and the reagent stream occurs in the crossbar of the H, not in the first channel as claimed in the present invention.

Nor does Wu *et al.* make any mention of a method for performing cell-based operations capable of identifying single cell status with fixed cells.

Accordingly, Applicants submit that the standard of strict identity required to maintain a rejection under 35 U.S.C. § 102 has not been met. Withdrawal of the rejection under 35 U.S.C. § 102(e) is respectfully requested.

V. Rejections under 35 U.S.C. §103

Claim 15 was rejected under 35 U.S.C. §103 as allegedly obvious over Wu *et al.* in view of Wiktorowicz *et al.* (U.S. Patent No. 6,013,165).

A. The Present Invention

The present invention is described above.

B. The Prior Art

WU ET AL. is described above.

WIKTOROWICZ ET AL. describe an apparatus for multi-dimensional electrophoresis of analytes. A single separation apparatus is used for electrophoresis in both dimensions. The apparatus has a plate assembly that defines a sample separation cavity bounded by opposing first and second surfaces. A sample that has been resolved in a first electrophoretic dimension can be directly electrophoresed in a second dimension that is substantially perpendicular to the first.

C. Analysis

According to the M.P.E.P. § 2143, "to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference

teachings. Second, there must be a reasonable expectation of success. Third, the prior art references (or references when combined) must teach or suggest all the claim limitations."

As discussed above, Wu *et al.* fail to teach element (i) of the present invention.

The teachings in Wiktorowicz *et al.* do not make up for the deficiencies in Wu *et al.*, as this reference is not concerned with methods for performing cell-based operations capable of identifying single cell status. Wiktorowicz *et al.* teach multi-dimensional electrophoresis of analytes where a sample that has been resolved in a first electrophoretic dimension can be directly electrophoresed in a second dimension that is substantially perpendicular to the first dimension.

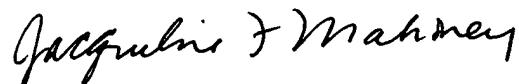
Therefore, none of the references alone or in combination teach all the claim limitations of the present invention, the standard for obviousness has not been met. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §103.

CONCLUSION

In view of the foregoing, Applicants submit that the claims pending in the application are in condition for Allowance. A Notice of Allowance is therefore respectfully requested.

The Examiner is invited to contact Applicants' representative at (650) 838-4410 if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted,



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